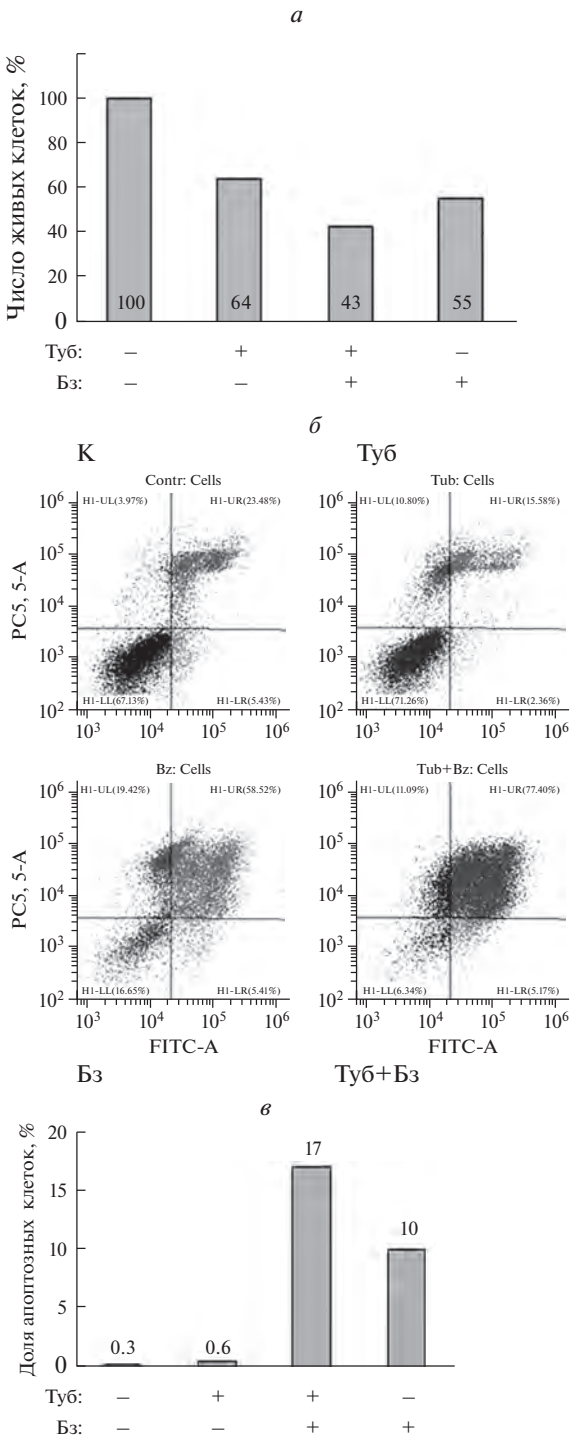

Рис. 8. Совместное действие тубацина (Туб, 15 мкМ) и бортезомиба (Бз, 15 нМ) значительно снижает жизнеспособность клеток mERas вследствие активации апоптоза. *а* – Жизнеспособность клеток, оцененная с помощью набора Count and Viability для цитометра Muse Cell Analyzer, (–) – контроль; процентное количество живых клеток указано внутри столбцов. *б* – Двупараметрическое распределение клеток (содержание ДНК против Аннексин V-FITC) по данным проточной цитометрии; показаны контрольные клетки (К), действие Туб, Бз, раздельно и совместно. *в* – Диаграмма по результатам одного из экспериментов, представленного в части *б* этого рисунка; показано процентное содержание апоптотических клеток.

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Tubacin, a Histone Deacetylase 6 Inhibitor, Causes α-Tubulin Acetylation, Cell Cycle Arrest, Senescence and Suppression of Migration of Mouse Fibroblasts Transformed by *E1A* and *cHa-ras* Oncogenes

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Inhibitors of histone deacetylase activity (HDACs) are widely used to block proliferation of cancer cells in clinical trials *in vivo* and in studies on tumor cell lines *in vitro*. Some inhibitors reached to the clinical stage (SAHA, Class I). In addition to the suppression of cancer cell proliferation, they are capable of inducing either cellular senescence or apoptotic cell death and autophagy. HDAC6 (Class II) is different from other HDACs in its cytoplasmic localization and the lack of a noticeable histone deacetylase activity. In turn, HDAC6 deacetylates a number of non-histone proteins, including α-tubulin, a component of microtubules, thereby influencing microtubule stability. Overexpression of HDAC6 has been identified in a variety of cancer cell lines and mouse tumor models. Available data suggest that HDAC6 is involved in quality control in the process of autophagy as α-tubulin acetylation is essential for fusion of autophagosomes to lysosomes. We compared the effects produced by HDAC inhibitor sodium butyrate, which inhibits the activity of HDACs Class I, but not HDAC6, and by Tubacin, which is a specific inhibitor of HDAC6. It turned out that Tubacin causes the same effects as the sodium butyrate does regarding suppression of cell growth, induction of G_1/S cell cycle arrest and cellular senescence. As long as Tubacin treatment induces acetylation of α-tubulin, one may suggest that the level of α-tubulin acetylation is indispensable for proliferation, senescence and cell migration of E1A + Ras transformed cells.

Keywords: mouse embryonic fibroblasts, HDAC6, tubacin, senescence, cell cycle, cell migration, apoptosis